

PATENT COOPERATION TREATY

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Commissioner
 US Department of Commerce
 United States Patent and Trademark
 Office, PCT
 2011 South Clark Place Room
 CP2/5C24
 Arlington, VA 22202
 ETATS-UNIS D'AMERIQUE
 in its capacity as elected Office

Date of mailing (day/month/year) 17 July 2001 (17.07.01)	
International application No. PCT/US00/25585	Applicant's or agent's file reference MCA-483 PC
International filing date (day/month/year) 18 September 2000 (18.09.00)	Priority date (day/month/year) 17 September 1999 (17.09.99)
Applicant FOLEY, Brian	

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:
 04 April 2001 (04.04.01)

☐ in a notice effecting later election filed with the International Bureau on:

2. The election ☒ was

☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No.: (41-22) 740.14.35	Authorized officer H. Zhou Telephone No.: (41-22) 338.83.38
--	--

PATENT COOPERATION TREATY

MO58 / KHE
CnFrom the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

KING, T.J.
HENKEL, FEILER & HÄNZEL
Möhlstrasse 37
81675 München
ALLEMAGNE

PTO/PCT Rec'd

07 FEB 2002

EINGEGANGEN

23.11.2001

PCT

NOTIFICATION OF TRANSMITTAL OF
THE INTERNATIONAL PRELIMINARY
EXAMINATION REPORT
(PCT Rule 71.1)Date of mailing
(day/month/year)

22.11.2001

Applicant's or agent's file reference
MCA-483 PC

IMPORTANT NOTIFICATION

International application No.
PCT/US00/25585International filing date (day/month/year)
18/09/2000Priority date (day/month/year)
17/09/1999Applicant
MILLIPORE CORPORATION

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.
2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.
3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. REMINDER

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/



European Patent Office
D-80298 Munich
Tel. +49 89 2399 - 0 Tx: 523656 epmu d
Fax: +49 89 2399 - 4465

Authorized officer

Fuerbass, C

Tel. +49 89 2399-8132



PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference MCA-483 PC	FOR FURTHER ACTION see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. PCT/US 00/ 25585	International filing date (day/month/year) 18/09/2000	(Earliest) Priority Date (day/month/year) 17/09/1999
Applicant MILLIPORE CORPORATION		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 3 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

- b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

☐ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☐ **Certain claims were found unsearchable** (See Box I).

3. ☐ **Unity of invention is lacking** (see Box II).

4. With regard to the **title**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No.

☒ as suggested by the applicant.

☐ because the applicant failed to suggest a figure.

☐ because this figure better characterizes the invention.

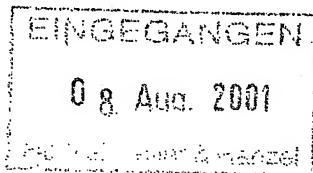
1
☐ None of the figures.

PATENT COOPERATION TREATY

From the:
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

KING, T.J.
HENKEL, FEILER & HÄNZEL
Möhlstrasse 37
81675 München
ALLEMAGNE



PCT

✓ 28.10.01 ✓

✓ 7.11.01 ✓

WRITTEN OPINION

(PCT Rule 66)

Applicant's or agent's file reference

MCA-483 PC

Date of mailing
(day/month/year)

07.08.2001

REPLY DUE

within 3 month(s)
from the above date of mailing

International application No.

PCT/US00/25585

International filing date (day/month/year)

18/09/2000

Priority date (day/month/year)

17/09/1999

International Patent Classification (IPC) or both national classification and IPC

B01D63/00

Applicant

MILLIPORE CORPORATION

1. This written opinion is the **first** drawn up by this International Preliminary Examining Authority.

2. This opinion contains indications relating to the following items:

- I ☒ Basis of the opinion
- II ☐ Priority
- III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☒ Certain document cited
- VII ☒ Certain defects in the international application
- VIII ☐ Certain observations on the international application

3. The applicant is hereby **invited to reply** to this opinion.

When? See the time limit indicated above. The applicant may, before the expiration of that time limit, request this Authority to grant an extension, see Rule 66.2(d).

How? By submitting a written reply, accompanied, where appropriate, by amendments, according to Rule 66.3. For the form and the language of the amendments, see Rules 66.8 and 66.9.

Also: For an additional opportunity to submit amendments, see Rule 66.4.
For the examiner's obligation to consider amendments and/or arguments, see Rule 66.4 bis.
For an informal communication with the examiner, see Rule 66.6.

If no reply is filed, the international preliminary examination report will be established on the basis of this opinion.

4. The final date by which the international preliminary examination report must be established according to Rule 69.2 is: 17/01/2002.

Name and mailing address of the International preliminary examining authority:

European Patent Office
D-80298 Munich
Tel. +49 89 2399 - 6 23656 epmu d
Fax: +49 89 2399 - 4465

Authorized officer / Examiner

Connor, M

Formalities office (incl. extension of time limits)

Fuerbass, O
Telephone No. +49 89 2399 8132



WRITTEN OPINION

International application No. PCT/US00/25585

I. Basis of the opinion

1. With regard to the **elements** of the international application (Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this opinion as "originally filed"):

Description, pages:

1-9 as originally filed

Claims, No.:

1-32 as originally filed

Drawings, sheets:

1/1 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:

WRITTEN OPINION

International application No. PCT/US00/25585

☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	1 (no)
Inventive step (IS)	Claims	1-32 (no)
Industrial applicability (IA)	Claims	1-32 (yes)

2. Citations and explanations
see separate sheet

VI. Certain documents cited

1. Certain published documents (Rule 70.10)

and / or

2. Non-written disclosures (Rule 70.9)

see separate sheet

VII. Certain defects in the international application

The following defects in the form or contents of the international application have been noted:
see separate sheet

Re Item V

Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

- 1 The following documents are referred to in the present opinion:

D1: WO 88 06723 A (BIONIQUE LAB INC) 7 September 1988 (1988-09-07)
D2: EP-A-0 272 043 (PALL CORP) 22 June 1988 (1988-06-22)

- 2 The product proposed in claim 1 of the present application cannot be considered as new (Article 33(2)PCT) for the following reasons.

D1 and D2 both disclose a multi-well filter according to the features called for in claim 1 of the present application, except for the feature: "not having been molded therein." Said feature, however, is not a technical feature of the product *per se*, but a **process** feature. The EPO-Guidelines, for instance, clearly state in Part C-III 4.7b that "a product is not rendered novel merely by the fact that it is produced by means of a [different] process." It follows that said feature is to be construed as "a multi-well filter obtainable by a process..."

In the present case, the process technique employed in D1 and D2 for the formation of the through holes is not disclosed. Considering for instance D1, the applicant will certainly agree that the conical holes of the device disclosed therein could perfectly well be produced by any available technique including both injection moulding and drilling. The skilled man could not determine the process used—in particular if the parts were properly ground and polished to remove any flash or cutting debris—and if he could, the differing feature would not confer the filter *per se* any particular advantage. Consequently, the product *per se* is not new in the sense of Article 33(2) PCT.

- 3 The method for producing a multi-well membrane filter proposed in claim 21 of the present application cannot be considered as involving an inventive step (Article 33(3) PCT) for the following reasons.

The subject matter of claim 21 of the present application differs from the disclosure of D1 and D2 in that neither document specifies how the through holes were formed. An economical comparison between injection moulding and alternative techniques (e.g., removing material from a given support) presented in the present application concluded that the alternative techniques according to the present

invention "can provide a multi-well membrane filter that is much cheaper on a per well basis than a prior art [injection moulded] multi-well membrane filter" (cf. p. 3, ll. 9-10), thus justifying the inventive step of the claimed method.

It must be argued, however, that any economical comparison between different process techniques must always be expressed as a function of production volume. For instance, drilling manually one by one each through hole falls within the scope of claim 21 and would probably yield a much cheaper multi-well filter than an injection moulded one for very low production volumes. On the other hand, upon increasing the production volume there will be a point where the injection moulded version will become cheaper than the hand-drilled one. The same applies to many alternative processes falling within the scope of claim 21.

Consequently, in the absence of a production volume and a better defined alternative process technique, no inventive step can be recognized to claim 21 of the present application.

- 4 Dependent claims 2-21 and 13-32 do not seem to contain any features which, in combination with the features of any claim to which they refer, meet the requirements of the PCT in respect of novelty and/or inventive step, on the basis of D1 and D2 and common knowledge of the skilled person.
- 5 The applicant is invited to file new claims taking account of the deficiencies mentioned in the present communication (see also points VII and VIII below) and to adapt the description accordingly. The application may not be amended in such a way that it contains subject-matter which extends beyond the content of the application as filed (Article 34(2)(b) PCT). In order to facilitate the examination of the conformity of the amended application with the requirements of Article 34(2)(b) PCT, the applicant is requested to clearly identify the amendments carried out, irrespective of whether they concern amendments by addition, replacement or deletion, and to indicate the passages of the application as filed on which these amendments are based. If the applicant regards it as appropriate these indications could be submitted in handwritten form on a copy of the relevant parts of the application as filed.

Re Item VI

Certain documents cited

- 1 The following document has been mentioned in the search report as a P-document:

D3: DE 199 04 784 A (DEUTSCHES KREBSFORSCH) 10 August 2000 (2000-08-10)

The validity of the priority date of the present application has not been checked. It must be mentioned, however, that D3 seems to disclose all the essential features called for in the claims of the present application.

Re Item VII

Certain defects in the international application

- 1 It is mentioned on p. 4, ll. 19-23 that the skilled person had a prejudice against producing the micro-well filter according to claim 21 because "the volume requirements would have necessitated a plate of a large thickness [...]. At such thickness, there is no motivation to using anything other than moulding due to costs of that process." It is not quite well understood what permitted the applicant to overcome said prejudice, and why would a skilled person use a plate of thickness > 0.5 inch and the applicant could suddenly decide to use thinner than 0.25 inch plates. The applicant is requested to justify said passage or to delete it.
- 2 The units of measure [inch] employed on page 4, ll. 19 and 21 is not additionally expressed in terms of the units stipulated by Rule 10.1(a)PCT.

INTERNATIONAL SEARCH REPORT

International Application No

T/US 00/25585

A. CLASSIFICATION OF SUBJECT MATTER
 IPC 7 B01D61/18

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 B01D C12M B01L

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P, X	DE 199 04 784 A (DEUTSCHES KREBSFORSCH) 10 August 2000 (2000-08-10) column 2, line 52-557 column 1, line 45-60 ---	1
A	US 5 843 767 A (BEATTIE KENNETH L) 1 December 1998 (1998-12-01) column 9, line 45 -column 11, line 55; figure 1A ---	1
A	WO 99 34920 A (MASSACHUSETTS INST TECHNOLOGY) 15 July 1999 (1999-07-15) page 6, line 27 -page 7, line 15; figure 5 ---	1
A	WO 88 06723 A (BIONIQUE LAB INC) 7 September 1988 (1988-09-07) page 7, line 23-29 --- -/--	27-32

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents :

A document defining the general state of the art which is not considered to be of particular relevance

E earlier document but published on or after the international filing date

L document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

O document referring to an oral disclosure, use, exhibition or other means

P document published prior to the international filing date but later than the priority date claimed

T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

X document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

Y document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

* & * document member of the same patent family

Date of the actual completion of the international search

26 February 2001

Date of mailing of the international search report

06/03/2001

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
 NL - 2280 HV Rijswijk
 Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
 Fax: (+31-70) 340-3016

Authorized officer

Zinngrebe, U

INTERNATIONAL SEARCH REPORT

International Application No

T/US 00/25585

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	EP 0 272 043 A (PALL CORP) 22 June 1988 (1988-06-22) abstract; figure 2 ---	1
A	US 5 342 581 A (SANADI ASHOK R) 30 August 1994 (1994-08-30) column 7, line 10-27 ---	1
A	WO 97 15394 A (BAINS WILLIAM ARTHUR ;HOUZEGO PETER JOHN (GB); SMITHKLINE BEECHAM) 1 May 1997 (1997-05-01) page 3, last paragraph -page 4, paragraph 4; figure 2A ---	1
A	WO 98 55852 A (SUNDBERG STEVEN A ;CHOW CALVIN Y H (US); PARCE J WALLACE (US); CAL) 10 December 1998 (1998-12-10) page 12, line 9-26 page 11, line 14-17 -----	1

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

T/US 00/25585

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
DE 19904784	A	10-08-2000	WO 0045950 A	10-08-2000
US 5843767	A	01-12-1998	AU 700315 B	24-12-1998
			AU 1043595 A	22-05-1995
			CA 2174140 A	04-05-1995
			EP 0725682 A	14-08-1996
			JP 9504864 T	13-05-1997
			WO 9511755 A	04-05-1995
WO 9934920	A	15-07-1999	AU 2102699 A	26-07-1999
			EP 1051259 A	15-11-2000
WO 8806723	A	07-09-1988	EP 0302933 A	15-02-1989
EP 0272043	A	22-06-1988	US 4797259 A	10-01-1989
			CA 1312265 A	05-01-1993
			DE 3780012 A	30-07-1992
			DE 3780012 T	21-01-1993
			GB 2198847 A, B	22-06-1988
			JP 1933639 C	26-05-1995
			JP 6064062 B	22-08-1994
			JP 63167267 A	11-07-1988
US 5342581	A	30-08-1994	AU 6552994 A	08-11-1994
			CA 2160478 A	27-10-1994
			EP 0737106 A	16-10-1996
			WO 9423839 A	27-10-1994
			US 5516490 A	14-05-1996
			US 5741463 A	21-04-1998
WO 9715394	A	01-05-1997	EP 0862497 A	09-09-1998
			JP 2000500567 T	18-01-2000
WO 9855852	A	10-12-1998	US 6090251 A	18-07-2000
			AU 7820798 A	21-12-1998
			EP 0988530 A	29-03-2000
			US 6086825 A	11-07-2000

PATENT COOPERATION TREATY

PCT

REC'D 27 NOV 2001

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference MCA-483 PC	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/US00/25585	International filing date (day/month/year) 18/09/2000	Priority date (day/month/year) 17/09/1999
International Patent Classification (IPC) or national classification and IPC B01D63/00		
Applicant MILLIPORE CORPORATION		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.



2. This REPORT consists of a total of 9 sheets, including this cover sheet.

- ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of 4 sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☒ Certain documents cited
- VII ☒ Certain defects in the international application
- VIII ☒ Certain observations on the international application

Date of submission of the demand 04/04/2001	Date of completion of this report 22.11.2001
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Connor, M Telephone No. +49 89 2399 8402 

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/US00/25585

I. Basis of the report

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

Description, pages:

1-3,5-9	as originally filed		
4	as received on	06/11/2001 with letter of	06/11/2001

Claims, No.:

1-32	as originally filed		
33-45	as received on	06/11/2001 with letter of	06/11/2001

Drawings, sheets:

1/1	as originally filed
-----	---------------------

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/US00/25585

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	
	No:	Claims	1,21,33
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-45
Industrial applicability (IA)	Yes:	Claims	1-45
	No:	Claims	

2. Citations and explanations
see separate sheet

VI. Certain documents cited

1. Certain published documents (Rule 70.10)

and / or

2. Non-written disclosures (Rule 70.9)

see separate sheet

VII. Certain defects in the international application

The following defects in the form or contents of the international application have been noted:
see separate sheet

VIII. Certain observations on the international application

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/US00/25585

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:
see separate sheet

Re Item I

Basis of the report

1 The amendments filed with the applicant's letter dated 06.11.2001 introduce subject matter that goes beyond the disclosure of the initially filed application contrary to Article 34(2)(b) PCT.

1.1 Claim 35 calls for a method comprising the following sequence of operations carried out on a continuous web: (a) forming the through holes; (b) attaching the filter membrane; and (c) subsequently cutting the device to a desired size.

No basis could be found in the originally filed application to support the full sequence (a)-(b)-(c). On p. 5, ll. 29-30, the following steps are disclosed: "the perforated sheet could be presented to the assembly machine [...] as a continuous web and cut to size on line". All that can be concluded from said passage is that perforation occurs prior to cutting, but nothing can be said concerning the order in which the perforated sheet is cut and laminated to a filter membrane.

1.2 claim 38 calls for a method comprising the step of making the area around the individual through holes impervious to a filtrate **immediately before** the attaching step. Page 8, l. 11 reads "collapsing the pores **prior** to laminating"; the term "prior" cannot justify the expression "immediately before." The term "before" used alone would be admissible under Article 34(2)(b) PCT.

Re Item V

Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1 The following documents are referred to in the present opinion:

- D1: WO 88 06723 A (BIONIQUE LAB INC) 7 September 1988 (1988-09-07)
- D2: EP-A-0 272 043 (PALL CORP) 22 June 1988 (1988-06-22)
- D3: US-A-5 843 767 (BEATTIE KENNETH L) 1 December 1998 (1998-12-01)

2 The product proposed in claim 1 of the present application cannot be considered as new (Article 33(2)PCT) for the following reasons.

2.1 D3 discloses a multi-well membrane filter comprising a support with through holes (cf. D3, Fig. 3, upper part marked "SiO₂"), and a membrane fixed to said support as

described in claim 1 (cf. D3, Figure 3, element marked "Si" and col. 12, ll. 22 ff.). A porous silicone wafer can certainly be defined as a porous "membrane filter". The through holes were not moulded therein as explained in col. 13, ll. 24-41.

- 2.2 D1 and D2 both disclose a multi-well filter according to the features called for in claim 1 of the present application, except for the feature: "not having been molded therein." Said feature, however, is not a technical feature of the product *per se*, but a **process** feature. The EPO-Guidelines, for instance, clearly state in Part C-III 4.7b that "a product is not rendered novel merely by the fact that it is produced by means of a [different] process." It follows that said feature is to be construed as "a multi-well filter obtainable by a process..."

In the present case, the process technique employed in D1 and D2 for the formation of the through holes is not disclosed. Considering for instance D1, the applicant will certainly agree that the conical holes of the device disclosed therein could perfectly well be produced by any available technique including both injection moulding and drilling. The skilled man could not determine the process used—in particular if the parts were properly ground and polished to remove any flash or cutting debris—and if he could, the differing feature would not confer the filter *per se* any particular advantage. Consequently, the product *per se* is not new in the sense of Article 33(2) PCT.

- 3 The method for producing a multi-well membrane filter proposed in claim 21 of the present application cannot be considered as novel and as involving an inventive step (Article 33(2)&(3) PCT) for the following reasons.

- 3.1 The subject matter of claim 21 is anticipated by the disclosure of D3, col. 13, ll. 24-49 (Article 33(2) PCT).

- 3.2 The subject matter of claim 21 of the present application differs from the disclosure of D1 and D2 in that neither document specifies how the through holes were formed. An economical comparison between injection moulding and alternative techniques (e.g., removing material from a given support) presented in the present application concluded that the alternative techniques according to the present invention "can provide a multi-well membrane filter that is much cheaper on a per well basis than a prior art [injection moulded] multi-well membrane filter" (cf. p. 3, ll. 9-10), thus

justifying the inventive step of the claimed method.

It must be argued, however, that any economical comparison between different process techniques must always be expressed as a function of production volume. For instance, drilling manually one by one each through hole falls within the scope of claim 21 and would probably yield a much cheaper multi-well filter than an injection moulded one for very low production volumes. On the other hand, upon increasing the production volume there will be a point where the injection moulded version will become cheaper than the hand-drilled one. The same applies to many alternative processes falling within the scope of claim 21.

Consequently, in the absence of a production volume and a better defined alternative process technique, no inventive step can be recognized to claim 21 of the present application Article 33(3) PCT).

4 The method proposed in claim 33 of the present application cannot be considered as novel (Article 33(2) PCT) for the following reasons.

4.1 D3 discloses a method for producing a multi-well membrane filter device comprising:

- (a) selecting a pre-formed individual support sheet of predetermined thickness: cf. D3, col. 13, ll. 26-28;
- (b) selectively forming through holes corresponding to the desired well configuration and in a desired well matrix array in the support sheet by a material removing process: cf. D3, col. 13, ll. 28-41;
- (c) attaching a filter membrane by a laminating process to one side of the support sheet provided with the through holes: cf. D3, col. 13, ll. 41-44.

The disclosure of D3 thus anticipates the subject matter of claim 33 of the present application.

4.2 Neither D1 nor D2 discloses any processing method. Once again, as mentioned in point V-3.2 supra, the choice by the skilled person to manufacture the well plate by injection moulding is greatly dependent on the production volume, since injection moulding tools per se are very expensive. One particular case where a skilled person would certainly not injection mould the well plate is the prototyping stage of a newly developed product. A single or low series prototype is produced for testing and

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/US00/25585

modifying design features not directly apparent at the designing stage. In this case, the individual pre-formed parts are generally machined. This would probably not encompass the embodiment of the "continuous support sheet".

- 5 Dependent claims 2-21, 13-32, and 34-45 do not seem to contain any features which, in combination with the features of any claim to which they refer, meet the requirements of the PCT in respect of novelty and/or inventive step, on the basis of D1, D2, and D3 and common knowledge of the skilled person.

Re Item VI

Certain documents cited

- 1 The following document has been mentioned in the search report as a P-document:

D4: DE 199 04 784 A (DEUTSCHES KREBSFORSCH) 10 August 2000 (2000-08-10)

The validity of the priority date of the present application has not been checked. It must be mentioned, however, that D3 seems to disclose all the essential features called for in the claims of the present application.

Re Item VII

Certain defects in the international application

- 1 It is mentioned on p. 4, ll. 19-23 that the skilled person had a prejudice against producing the micro-well filter according to claim 21 or 33 because "the volume requirements would have necessitated a plate of a large thickness [...]. At such thickness, there is no motivation to using anything other than moulding due to costs of that process."
- 1.1 It is not quite well understood from the description what permitted the applicant to overcome said prejudice, and why would a skilled person use a plate of thickness > 12.7 mm (0.5 inch) and the applicant could suddenly decide to use thinner than 6.4 mm (0.25 inch) plates. Moreover, if any excess thickness could be problematic for embodiments comprising e.g., punching, it is not clear that so is the case for other embodiments of the claimed invention such as drilling.
- 1.2 D2, col. 3, ll. 54-57 discloses wells of diameter preferably comprised between 2 and

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/US00/25585

25 mm and height between 5 and 10 mm. Five millimetre deep wells are shallower than 6.25 mm mentioned in the foregoing passage, and the well volume assuming a cylindrical geometry with 2 mm diameter yields 16-31 μl for 5 and 10 mm height, respectively which is smaller than the well volumes called for in claims 16, 17, and 43.

- 1.3 It would appear from the foregoing discussion that the alleged prejudice referred to on p. 4, ll. 19-23 is not justified and should therefore be deleted.

Re Item VIII

Certain observations on the international application

- 1 Claim 33 comprises all the features of claim 21 (except "suitable for filtering solutions in a laboratory setting") and should therefore be drafted as a claim dependent on the latter.
- 2 Claim 37 lacks clarity in the sense of Article 6 PCT since "diffusion bonding" and "thermal bonding" are special embodiments of the more general term "welding". It could be amended to read "welding by diffusion or thermal bonding".

Henkel, Feiler & Hänzle

10/049537
JC12 Rec'd PCT/PTO 07 FEB 2002
Patentanwälte

European Patent Attorneys
Zugelassene Vertreter vor dem
Europäischen Patentamt
und dem Harmonisierungsamt

Dr. phil. G. Henkel +
Dr. rer. nat. L. Feiler
Dipl.-Ing. W. Hänzle
Dipl.-Ing. M. Garkisch
Dr. rer. nat. Chr. Schön
Dr. rer. nat. E. Wenning

Möhlstraße 37
D-81675 München

Telefon: +49-89-98 20 85
Telefax: +49-89-98 14 26 (G3)
Telefax: +49-89-98 105 995 (G3/4)
E-mail: mail@henkelpatent.de

Europäisches Patentamt

als I P E A

Erhardtstr. 27

80298 München

November 6, 2001

International Application No. PCT/US00/25585
MILLIPORE CORPORATION
Our Ref.: 11058/ME/wg/st

To the Written Opinion pursuant to PCT Rule 66 dated August 7,
2001

In response to the Written Opinion we respectfully submit in triplicate new claims 33 to 45 and a new description page 4. The new claims are to be appended to the originally filed set of claims and the new description page 4 is to replace the current description page 4.

Amendments:

The new claims 33 to 45 are directed to a method of producing a multi-well membrane filter device. The claims are based on the former method claims but have been clarified and worded as true method claims.

The new claim 33 is based on former claim 21. The features that the support sheets can be either individual or continuous sheets of a predetermined thickness is supported by the description on page 5, lines 28 to 30 and page 6, lines 5 to 8.

The new claim 34 is based on current claim 22.

The new claim 35 in more detail defines the features of producing the multi-well membrane filter device in a continuous process.

The new claim 36 is a combination of current claims 23 to 26.

The new claim 37 is a combination of current claims 27 to 31.

The new claim 38 is based on current claim 32. The feature that the making of the areas impervious to the filtrate is carried out after, immediately before or simultaneously with the attaching step is supported by the description on page 7, line 30, page 8, lines 12/13 and page 8, line 18 for the various alternatives.

The new claim 39 is supported by the description on page 8, lines 8 to 26.

The new claim 40 is based on current claim 19.

The new claim 41 is based on current claims 2 to 7.

The new claim 42 is based on current claims 8 to 12.

The new claim 43 is based on current claims 16 and 17.

The new claim 44 is based on current claim 18 and the new claim 45 is based on current claims 13 and 14.

The current claims 1 to 32 are maintained in this application for the reason that amendments to the claims might be interpreted differently in the various countries covered by this application. It is nevertheless respectfully requested to also provide the IPER on the set of claims including these new claims in order to be able to appropriately select the claims which are to be prosecuted in the respective national/regional phases.

Patentability:

We disagree with the Examiner's conclusion that the method of producing a multi-well membrane filter device of the present invention is obvious in view of regular skill in the general manufacturing technology.

Specifically, the method of the present invention is based on first selecting a pre-formed individual or continuous support sheet of a predetermined thickness. In this support sheet through holes are formed by a material removing process. Then, a filter membrane is laminated to one side of the support sheet provided with the through holes. In consequence, the wells are formed and surrounded by the circumferential wall of the through holes and by the filter membrane attached to and closing one side of the through holes.

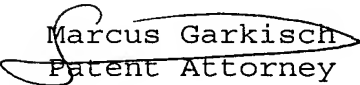
In the prior art multi-well membrane filter devices of this type commonly are manufactured by injection molding. The present invention leaves this well established teaching and provides an alternative new method which is extremely cost effective for large scale production. Economical considerations in this respect must be regarded as relevant only for the decision whether or not a particular process is applied and to determine the actual cost of a product made by a particular process after it has been selected. It is not prejudicial to the fact whether and how particular products can be manufactured with a particular manufacturing process in technical aspects.

As the prior art does not contain particular or specific hints directed to the technical aspects of the method of the present invention of producing a particular product, i.e. a multi-well membrane filter device, we believe that the method is neither anticipated nor suggested by the prior art in an obvious manner.

Therefore, the originally filed and the new method claims 21 to 45 are considered to meet the requirements of novelty and inventive step.

With respect to the document DE 199 04 784 A (D3) it is respectfully pointed out that this document teaches micro assays formed of four different layers, a top plate, a membrane, a well plate and a bottom vacuum plate. These layers are held together with clamps (see column 2, lines 29 to 32). Therefore, this document appears to be not particularly relevant with respect to the present invention which teaches to form through holes by a material removing process in the support sheet and laminating, i.e. fixedly attaching a filter membrane directly to one side of the support sheet.

With respect to the objection in item 7, point 1 it is pointed out that in the prior art and in the every day practice in the industry it is conventional wisdom that one needs a large volume in each well of a multi-well filter device to filter the respective materials. As the plates are by convention of a uniform width and length, such large volume only can be achieved by increasing the depth or the diameter of the wells. As mentioned above, the only method previously applied for manufacturing such structures is injection molding. The applicant has discovered that large volumes of the wells are not necessarily required, especially with high throughput screening. The device of this invention is therefore part of a more complex development of procedures in connection with filtration which utilize lower volumes of material. The statement referred in item VII. point 1 is directed to this development. Therefore it appears to be justified.


Patent Attorney

Encl.:
New claims 33-45, 3-fold
New description page 4, 3-fold

PCT/US00/25585
MILLIPORE CORPORATION

New Claims (proposal)

1. A method of producing a multi-well membrane filter device, comprising the steps of:

selecting a pre-formed individual or continuous support sheet of a predetermined thickness;

5 selectively forming through holes corresponding to a desired well configuration and in a desired well matrix array into the support sheet by a material removing process;

attaching a filter membrane by a laminating process to one side of the support sheet provided with the through
10 holes.

2. The method of claim 1, comprising the step of extruding a material to form the pre-formed individual support sheet.

15 3. The method of claim 1, comprising the step of maintaining the support sheet as continuous web during the steps of forming the through holes and attaching the filter membrane and subsequently cutting the device to a desired size.

20 4. The method of claim 1, 2 or 3, wherein the material removing process applied in the step of selectively forming the through holes into the support sheet is one selected of the following: drilling, punching, burning, dissolving.

25 5. The method of any one of claims 1 to 4, wherein the laminating process for attaching the filter membrane to the support sheet is one selected of the following: a web converting process, diffusion bonding, adhesive bonding,
30 welding, thermal bonding.

6. The method of any one of claims 1 to 5, comprising the step of making the areas of the filter membrane around the individual through holes impervious to a filtrate, wherein this step is performed after, immediately before or simultaneously with the attaching step.

7. The method of claim 6, wherein the step of making the areas of the filter membrane around the individual through holes impervious to a filtrate is one selected of the following: collapsing pores in the filter membrane, breaking or removing filter membrane, applying a hydrophobic barrier, filling membrane pores with epoxy.

8. The method of any one of claims 1 to 7, comprising the step of laminating an underdrain layer to the outer surface of the filter membrane.

9. The method of any one of claims 1 to 8, wherein the pre-formed individual or continuous support sheet is selected from the following materials: glass, metallic materials, ceramic materials, elastomeric materials, coated cellulosic materials, polymeric materials

10. The method of claim 9, wherein the polymeric material for the pre-formed individual or continuous support sheet includes: polyethylene, acrylic, PTFE, polycarbonate, styrene.

11. The method of any one of claims 1 to 10, wherein a volume of the wells defined by the configuration of the through holes and the thickness of the support sheet is in the range of 50 to 150 microliters, preferably in the range of 70 to 130 microliters.

12. The method of any one of claims 1 to 11, wherein at least two of the through holes on a filter device have different configurations.

13. The method of any one of claims 1 to 12, wherein the well array of a filter device comprises at least 96 wells, preferably at least 384 wells.

International Patent Application PCT/US00/25585
MILLIPORE CORPORATION

Comment on the Written Opinion under PCT Rule 66 dated August 7,
2001

In this first Communication during the International Preliminary Examination Procedure the Examiner in item 2 objects to the current device claims for not being new with respect to essentially all prior multi-well membrane filter devices. The basis of his opinion is that the device per se must be physically or structurally distinguished from prior art devices.

It appears to be difficult to counter this argument as the essential aspects of the present invention appear to result in a manufacturing process rather than in the device as such.

Although the Examiner in item 3 objects to the method claims for being obvious in view of regular skill we are of the opinion that this objection regarding the method claims is not well founded and should be countered.

For your convenience we have prepared the enclosed set of method claims which is based on the former claims and wherein the various previous dependent claims have been combined to reduce the total number of claims and to improve clarity. We also included additional dependent method claims to cover certain aspects of the previous device claims.

Please consider our proposed claims and advise whether they are acceptable or whether you wish to make amendments to the claims. Please also advise whether we should prosecute only the method claims or whether we should even continue with device claims during the international procedure in view of possible national/regional phases in the future.

Lastly, we would appreciate receiving your counter arguments to the Examiner's objections from your technical background in this specific field.

PCT/US00/25585
MILLIPORE CORPORATION

New Claims 33 to 45

33. A method of producing a multi-well membrane filter device, comprising the steps of:

selecting a pre-formed individual or continuous support sheet of a predetermined thickness;

5 selectively forming through holes corresponding to a desired well configuration and in a desired well matrix array into the support sheet by a material removing process;

10 attaching a filter membrane by a laminating process to one side of the support sheet provided with the through holes.

34. The method of claim 33, comprising the step of extruding a material to form the pre-formed individual support sheet.

15 35. The method of claim 33, comprising the step of maintaining the support sheet as continuous web during the steps of forming the through holes and attaching the filter membrane and subsequently cutting the device to a desired size.

20 36. The method of claim 33, 34 or 35, wherein the material removing process applied in the step of selectively forming the through holes into the support sheet is one selected of the following: drilling, punching, burning, dissolving.

25 37. The method of any one of claims 33 to 36, wherein the laminating process for attaching the filter membrane to the support sheet is one selected of the following: a web converting process, diffusion bonding, adhesive bonding,
30 welding, thermal bonding.

38. The method of any one of claims 33 to 37, comprising the step of making the areas of the filter membrane around the individual through holes impervious to a filtrate, wherein this step is performed after, immediately before or simultaneously with the attaching step.

39. The method of claim 38, wherein the step of making the areas of the filter membrane around the individual through holes impervious to a filtrate is one selected of the following: collapsing pores in the filter membrane, breaking or removing filter membrane, applying a hydrophobic barrier, filling membrane pores with epoxy.

40. The method of any one of claims 33 to 39, comprising the step of laminating an underdrain layer to the outer surface of the filter membrane.

41. The method of any one of claims 33 to 40, wherein the pre-formed individual or continuous support sheet is selected from the following materials: glass, metallic materials, ceramic materials, elastomeric materials, coated cellulosic materials, polymeric materials

42. The method of claim 41, wherein the polymeric material for the pre-formed individual or continuous support sheet includes: polyethylene, acrylic, PTFE, polycarbonate, styrene.

43. The method of any one of claims 33 to 42, wherein a volume of the wells defined by the configuration of the through holes and the thickness of the support sheet is in the range of 50 to 150 microliters, preferably in the range of 70 to 130 microliters.

44. The method of any one of claims 33 to 43, wherein at least two of the through holes on a filter device have different configurations.

45. The method of any one of claims 33 to 44, wherein the well array of a filter device comprises at least 96 wells, preferably at least 384 wells.

BRIEF DESCRIPTION OF THE FIGURES

Figure 1 provides top and sectional views of a multi-well filter device with different well shapes and an underdrain laminated thereto

5

DETAILED DESCRIPTION OF THE SPECIFIC EMBODIMENT

The present invention provides a multi-well membrane filter, the filter comprising a support characterized by through holes not having been molded therein; and a membrane filter fixed to said support so at least one side of at least two such through
10 holes are covered such that the device has at least two wells suitable for receiving material to be assayed.

Preferably, the support may be made of glass, metallic materials, ceramic materials, elastomeric materials and coated cellulosic materials. In a more preferable
15 embodiment, the support includes polymeric material. Polymeric materials suitable for the present invention include polyethylene, acrylic, PTFE, polycarbonate and styrene.

Preferably, the plate height is less than ^{6.4 mm} (one quarter inch) thick. The prior made no
20 suggestion for the plate of the present invention because the volume requirements would have necessitated a plate of a large thickness, i.e., ^{12.7 mm} greater than (one half inch). At such thickness, there is no motivation to using anything other than molding due to the costs of that process.

25 Preferably, the multi-well membrane filter of the present invention is configured to have at least 96 wells. In such a configuration, wells in a specific device may have different volumes. Preferably, individual wells have a volume in the range of 50 to 150 microliters. More preferably, the individual wells have a volume in the range of 70 to 130 microliters. For the 384-well format, a volume of about 100 to 120
30 microliters is preferred. It is envisioned that for formats greater than the 384-well format, the volume requirements will diminish. The wells may also have different shapes.